P-300

Systematic Methods of Scientific Discovery

Papers from the 1995 AAAI Symposium

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March 27 – 29, Stanford, California
Technical Report SS-95-03

AAAI Press
Menlo Park, California

Notes on Systematic Hypothesis Generation, and Application to Disciplined Brainstorming

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The DENDRAL project was a successful exemplar of the use of systematic planning, hypothesis generation, and pruning in confrontation with the data, for automated inference. At this time, my colleagues and I are exploring how this paradigm may relate to other examples of experiment planning and of scientific inference.

DENDRAL exemplified how abduction (in Peirce's sense: human intuition eliciting trial solutions) could be mirrored on the computer with

- exhaustive generation of hypotheses (candidate molecules) – for efficiency and discipline these should also be irredundant (which implies we have a test of iso-semantic equivalence)
- pruning strategies – exploiting the data and intermediate computations to tame the combinatorial expansion
- deductive confrontations – is a given candidate consistent with the observed MS (mass spectrum) data set?

Buried within the program were engineered innumerable substrategems: interactive displays of intermediate results, and justifications for the choices made at any point in the decision trees; user options to mark either mandated or proscribed substructures reshuffling the priority ordering of the nodes of the expansion.

Only in special cases did we implement problem decomposition: guessing which peaks reflected major binary cleavages of the input molecular ion, and attempting to solve these seriatim. The hardware technology of tandem MS-MS greatly enhances the power of that approach.

DENDRAL is of course a greatly simplified and stereotyped challenge. The range of hypotheses is the universe of possible organic molecules. This is immense but far more well-ordered than the sentences of broader scientific discourse. The isosemantic problem is reduced to mathematical graph automorphisms: and this in turn provoked some interesting theory of chemical graphs that made DENDRAL interesting and useful whatever one thought of the general machinery of artificial intelligence.

So, now we seek to generalize from this model to other experimental situations, and therein ask about the role of hypothesis elaboration, and so forth. What follows may be elementary to the point of tedium: that is the penalty of systematic, computable explicitness.

A generalized experimental model

A great many experimental protocols are built from the kernel (often greatly compounded and concatenated) in Figure 1. We take the right hand side, $P \rightarrow Q$ as not problematical. If it is, as in working out new analytical methods, then $P \rightarrow Q$ has to be treated as a separate experimental kernel.

Quite often, any real experimental process is multistaged, and the kernels (or nodes) may be concatenated and forked, perhaps even cyclized. Especially in vivo, the product of one reaction is the substrate of the next. We generally attempt to isolate one kernel as the problematic focus of attention, and hold the rest constant – always keeping in mind the latent need to reexamine what is now stipulated. A number of computational strategies have been devised to deal with compounding: forward and backward chaining; backtracking: languages like PROLOG have these facilities built in.

At each level we have Q = f(R,S,T). That is, R or S or T (or any combination) may be the independent variable on which we focus our interest. If it is T, the theory (or rule) for the process, then any instantiation where Q = f(R,S) conforms to the expected result is a corroboration of T. In a Popperian sense, we strive to qualify R and S to be maximally sensitive to deviations of T, to offer the best opportunity for disconfirmation of T. In DENDRAL, we are scanning over S. R is more or less fixed by the instrumentation, *pace* some evolving nuances of mass spectroscopy – e.g. chemical ion impact reaction MS. T, the rules of mass spectroscopy, are a body of empirical lore tempered with some modest theory of radical ion instability. Meta-DENDRAL was an early effort to abduce T, the rules of mass spectrometry, from data sets available: 2-ples of (S,Q).

To bring the ranges of R and S within the bounds of common sense, we have some "theory of the theories",

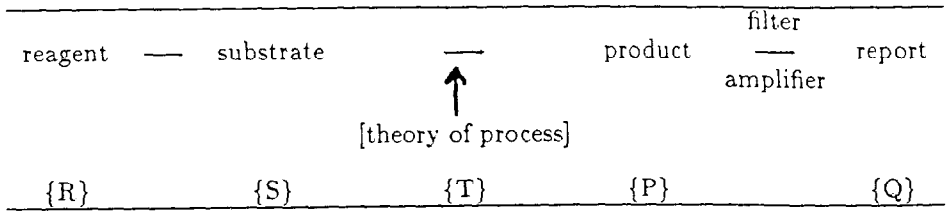

Figure 1: Kernel of Many Experimental Protocols

some notion of which R,S are most cogently related to T. We often have some intuitively derived instance, say R1,S1. Many experimenters stop there. A very powerful heuristic is to ask: what is the minimally relevant attribute of R1? Can we use that to generate all possible R's in that same set of neighbors? That often suggests very different lines of further inquiry. That heuristic I call avoiding, or reversing, *premature specification*. History would point us to many examples of how this has engendered grand fallacies: e.g. how Newtonian mechanics gives way to relativity and to quantum mechanics as we accelerate in velocity or diminish the size of the object.

In molecular biology, we point to the discovery of reverse transcription (RNA $\Rightarrow$ DNA), and of ribozymes (RNA vs protein as enzymes) in the same light. My presentation will give further examples of such stumbling blocks, and a progress report on our efforts towards generalization on the DENDRAL model.